Pedersen and Mathupala

Application No.: 09/808,743

Filed: March 14, 2001 Page 2

Attorney Docket No.: JHU1720-1

PATENT

I. AMENDMENTS

Please amend claims 1 and 27, as set forth below. Upon entry of the amendment, the status of the claims will be as follows:

- 1. (Currently Amended) A method of inhibiting proliferation of tumor cells characterized by having a highly glycolytic phenotype comprising contacting the cells with a proliferation inhibitory effective amount of an antisense polynucleotide or oligonucleotide that hybridizes with a mRNA encoding a hexokinase under conditions that allow hybridization of the antisense polynucleotide with the mRNA and inhibits hexokinase gene expression, thereby inhibiting the proliferation of tumor cells.
- 2. (Original) The method of claim 1, wherein the mRNA encoding hexokinase has a nucleotide sequence complementary to a sequence as set forth in SEQ ID NO:1.
 - 3. (Original) The method of claim 1, wherein the hexokinase is Type II hexokinase.
 - 4. (Withdrawn) The method of claim 1, wherein the hexokinase is Type I hexokinase.
- 5. (Withdrawn) The method of claim 1, wherein the mRNA encoding hexokinase has a nucleotide sequence complementary to a sequence as set forth in SEQ ID NO:2.
- 6. (Original) The method of claim 1, wherein the antisense polynucleotide or oligonucleotide comprises at least one modified internucleoside linkage.
- 7. (Original) The method of claim 6, wherein the modified internucleoside linkage is a phosphorothioate linkage.

Pedersen and Mathupala

Application No.: 09/808,743

Filed: March 14, 2001

Page 3

8. (Original) The method of claim 1, wherein the antisense oligonucleotide comprises at

PATENT

Attorney Docket No.: JHU1720-1

least one modified sugar moiety.

9. (Original) The method of claim 8, wherein the modified sugar moiety is a

2'-O-methoxyethyl sugar moiety.

10. (Original) The method of claim 1, wherein the antisense oligonucleotide comprises

at least one modified nucleobase.

11. (Original) The method of claim 10, wherein the modified nucleobase is a

5-methylcytosine.

12. (Original) The method of claim 1, wherein the antisense oligonucleotide is a

chimeric oligonucleotide.

13. (Original) The method of claim 1, wherein the tumor cells are located in a tissue

selected from the group consisting of brain, colon, urogenital, lung, renal, prostate, pancreas,

liver, esophagus, stomach, hematopoietic, breast, thymus, testis, ovarian, and uterine tissue.

14. (Original) The method of claim 1, wherein prior to treating tumor cells with the

antisense polynucleotide or oligonucleotide, the cells are diagnosed as highly glycolytic by

obtaining a specimen selected from the group consisting of serum, urine, saliva, blood,

cerebrospinal fluid, pleural fluid, ascites fluid, sputum, stool, bone marrow and biopsy sample.

15. (Previously Presented) The method of claim 1, wherein said tumor cells comprise

tumor cells of a low grade astrocytoma, anaplastic astrocytoma, glioblastoma, medulloblastoma,

Gray Cary\GT\6403303.2

Pedersen and Mathupala

Application No.: 09/808,743

Filed: March 14, 2001

Page 4

gastric cancer, hepatoma, colorectal cancer, colorectal adenoma, acute myelogenous leukemia,

PATENT

Attorney Docket No.: JHU1720-1

lung cancer, renal cancer, leukemia, breast cancer, prostate cancer, endometrial cancer, bone

cancer, squamous cell cancer or neuroblastoma.

16. (Original) A method of modulating the expression of a hexokinase in a tumor

characterized as having a highly glycolytic phenotype comprising contacting tumor cells or tissue

with an antisense polynucleotide or oligonucleotide that hybridizes with the hexokinase encoding

mRNA such that hexokinase enzyme translation is inhibited.

17. (Withdrawn) A pharmaceutical preparation useful for inhibiting proliferation of

tumor cells comprising an antisense polynucleotide that hybridizes with a mRNA encoding a

hexokinase in a pharmaceutically effective carrier.

18. (Withdrawn) the pharmaceutical preparation of claim 17, wherein the antisense

polynucleotide has a sequence complementary to the sequence set forth in SEQ ID NO:1.

19 to 26. (Cancelled)

27. (Currently Amended) A method of inhibiting proliferation of tumor cells

characterized by having a highly glycolytic phenotype due to a Type I hexokinase or a

Type II hexokinase, comprising contacting the cells with a proliferation inhibitory effective

amount of an antisense polynucleotide or oligonucleotide that hybridizes with a mRNA encoding

the Type I hexokinase or the Type II hexokinase under conditions that allow hybridization of the

antisense polynucleotide with the mRNA and inhibits hexokinase gene expression, thereby

inhibiting the proliferation of tumor cells.

Gray Cary\GT\6403303.2 104659-63

Pedersen and Mathupala

Application No.: 09/808,743

Filed: March 14, 2001 Page 5

Attorney Docket No.: JHU1720-1

PATENT

- 28. (Previously Presented) The method of claim 27, wherein the mRNA encoding the hexokinase has a nucleotide sequence complementary to a sequence as set forth in SEQ ID NO:1.
- 29. (Withdrawn) The method of claim 27, wherein the mRNA encoding the hexokinase has a nucleotide sequence complementary to a sequence as set forth in SEQ ID NO:2.
- 30. (Previously Presented) The method of claim 27, wherein the antisense polynucleotide or oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar moiety, or at least one modified nucleobase.
- 31. (Previously Presented) The method of claim 27, wherein the antisense oligonucleotide is a chimeric oligonucleotide.
- 32. (Previously Presented) The method of claim 27, wherein the tumor cells are located in brain, colon, urogenital tissue, lung, renal tissue, prostate, pancreas, liver, esophagus, stomach, hematopoietic tissue, breast, thymus, testis, ovarian tissue, or uterine tissue.
- 33. (Previously Presented) The method of claim 27, wherein said tumor cells comprise tumor cells of a low grade astrocytoma, anaplastic astrocytoma, glioblastoma, medulloblastoma, gastric cancer, hepatoma, colorectal cancer, colorectal adenoma, acute myelogenous leukemia, lung cancer, renal cancer, leukemia, breast cancer, prostate cancer, endometrial cancer, bone cancer, squamous cell cancer or neuroblastoma.